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Hemoglobin Levels before and after Chemotherapy (Cisplatin-Paclitaxel) of Nasopharyngeal Cancer Patients at Prof. Dr. Margono Soekarjo Hospital

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Abstract

Introduction: The National Comprehensive Cancer Network recommends induction chemotherapy and concurrent chemoradiotherapy as one of the standard therapy for stage II-IVA nasopharyngeal cancer. The use of induction chemotherapy given before radiotherapy is an effective treatment strategy because it has a better level of adherence and facilitates early eradication of micro metastasis. Chemotherapy has a direct side effect of disruption of erythrocyte formation in the bone marrow and reduces the erythropoietin hormone in the kidney. Decreased hemoglobin levels exacerbate oxygen deficiency in tumours thereby increasing hypoxic cells and contributing to the development of radiotherapy resistance.
Objective: This research was conducted to find out the hemoglobin levels before and after chemotherapy (cisplatin-paclita). An analytical observational study with cross sectional method. The subjects were 36 nasopharyngeal cancer patients that gone through 6 cycles of chemotherapy and meets the research criteria.xel in nasopharyngeal cancer patients.
Methods: An analytical observational studies with cross sectional method. The subjects were 36 nasopharyngeal cancer patients that gone through 6 cycles of chemotherapy and meets the research criteria.
Results: The results of the bivariate analysis showed differences in the average of hemoglobin levels before and after chemotherapy, the average hemoglobin levels before chemotherapy which were 13.39 g/dL and after chemotherapy which were 11.35 g /dL in nasopharyngeal cancer patients at Prof. Dr. Margono Soekarjo Hospital (P=0,001).
Conclusion: There is a significant difference between hemoglobin levels before and after chemotherapy (cisplatin-paclitaxel) in nasopharyngeal cancer patients in Prof. Dr. Margono Soekarjo Hospital.

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1. INTRODUCTION

The definition of nasopharyngeal cancer is squamous cell carcinoma arising from nasopharyngeal epithelium, futhermore the disease is bounded by geographical and racial distribution [1]. Globally, there are 80.000 new cases reported annually related to nasopharyngeal cancer [2]. Data in 2012 shows five countries that had the most deaths due to nasopharyngeal cancer were China (21,300 deaths), Indonesia (7,391 deaths), Vietnam (2,885 deaths), India (2,836 deaths), and Thailand (1,141 cases) [3]. The Global Cancer Observatory (GLOBOCAN) recorded in 2018 there were 17,992 new cases of nasopharyngeal cancer and the death rate reached 1,204 cases in Indonesia. Nasopharyngeal cancer occupies at the top 5 most frequently found new cancer cases in men, as many as 13,966 cases (8.7 %) in 2018 [4]. New nasopharyngeal cancer cases reported at RSUP Dr. Kariadi Semarang as many as 127 cases in the span years of 2000 to 2002 [5], had increased to 141 cases in 2014-2016 [6]. In Prof. Dr. Margono Soekarjo Hospital, nasopharyngeal cancer is the second most common type of malignancy found after cervical cancer [7]. Nasopharyngeal cancer cases in Prof. Dr. Margono Soekarjo Hospital reported as many as 497 cases in the span years of 2007 to 2016 [8].

Nasopharyngeal cancer therapy based on the National Comprehensive Cancer Network (NCCN) recommends induction chemotherapy and concurrent chemoradiotherapy as one of the standard treatments for stage II-IVA nasopharyngeal cancer. The use of induction chemotherapy given before radiotherapy is an effective treatment strategy because it has a better level of adherence and facilitates early eradication of micrometastasis [9]. Chemotherapy drugs are more effective when used in combination. Combination regimens that can be given with the platinum group include 5-fluorouracil, paclitaxel, and docetaxel. Combination cisplatin-paclitaxel chemotherapy produces higher clinical response rates than other drug combinations in particular [10].

Chemotherapy is a cytotoxic drug that has known to have myelosuppression side effects [11]. Chemotherapy cytotoxic agents can induce anemia through direct disorders of hematopoiesis, including the synthesis of erythrocyte precursors in the bone marrow and reducing erythropoietin production the kidney [12].

Decreased hemoglobin (Hb) levels might exacerbate oxygen deficiency in tumors thereby increasing hypoxic cells and contributing to the development of radiotherapy resistance. Low Hb levels have been reported as adverse factors in the management of radiotherapy from various tumors (ex., head and neck squamous cell cancer, cervical cancer, lung cancer, and bladder cancer) [13]. The lack of radiation optimization results in the repair of cancer cells that cause the therapeutic process becomes ineffective both technically, clinically, and economically. Anemia is dangerous state in patients as it has a higher risk of death rather than non anemic patients [14]. Thereafter, hemoglobin levels after chemotherapy induction can influence the choice and the outcome of further therapy. The authors expect the results of this study can serve as initial research on one of the side effects of chemotherapy combination, especially in bone marrow suppression by looking at hemoglobin levels in nasopharyngeal cancer patients.

2. MATERIALS AND METHODS

This observational analytic study was using cross sectional method with simple random sampling technique. The study was conducted using secondary data obtained from the ENT Installation of Prof. Dr. Margono Soekarjo Hospital from 2014 to 2019. Samples included in this study were stage II-IVA nasopharyngeal cancer patients who received combination chemotherapy cisplatin-paclitaxel within a period of 6 cycles. Criteria for exclusion of the study includes patients who were treated for radiation within 4 months before the initiation of chemotherapy, as well as incomplete medical record data of patients.

Data were analyzed using the SPSS program ver. 25. Bivariate analysis using paired t-test design with the aim of knowing the effects of chemotherapy in hematological toxicity, especially hemoglobin levels. The results are significant if P<0.05 was obtained.

3. RESULTS

This research data (36 samples) were obtained from medical records of nasopharyngeal patients who received cisplatin-paclitaxel chemotherapy in 2014 to 2019. Data collected were Hb levels, age, sex, nutritional status (BMI Score), and type of nasopharyngeal cancer obtained from medical record data.

Table 1. Baseline Characteristics of Research Subjects

Characteristics	Total (N=36)	Mean±SD	P-value
Sex, n (%)		1.14±0.351	**0.000**
Male	31(86.1)		
Female	5(13.9)		
Age, n (%)		1.61±0.494	**0.000**
≤40	6(16.7)		
>40	30(83.3)		
NPC Type, n (%)		2.78±0.422	**0.000**
WHO type I	0		
WHO type II	8(22.2)		
WHO type III	28(77.8)		
BMI, n (%)		1.83±0.507	**0.000**
Underweight	8(22.2)		
Normal	26(72.6)		
Overweight	2(5.6)		
Obese	0		
Hb Levels			
Before	36	13.397±2.0817	**0.691**
After	36	11.350±0.9467	**0.178**

Data distribution using the Shapiro-Wilk method shows Hb before chemotherapy (P=0.691) and Hb after chemotherapy (P=0.178). The data shows P>0.05 for Hb before and after chemotherapy, so it can be concluded that the Hb data before and after cis-pac chemotherapy in nasopharyngeal cancer patients were normally distributed. The results of the bivariate Paired Sample T-Test are displayed in the form of a mean, standard deviation, and p-value of hemoglobin levels shown in table 2.

Table 2. Mean and standard deviation of hemoglobin before and after chemotherapy

	Mean±SD	P-value
Hb Levels Before	13.397±2.0817	
Hb Levels After	11.350±0.9467	
Hb Before & After	2.0472±1.9726	0.001

Based on table 4, the mean Hb level in nasopharyngeal cancer patients before chemotherapy is 13,397 g/dL, with a minimum level of 9.3 g/dL and a maximum level of 18.5 g/dL. The mean Hb level in nasopharyngeal cancer patients after chemotherapy is 11.35 g/dL with a minimum level of 9.5 g/dL and a maximum level of 14.1 g/dL. After being tested using Paired Sample T-Test the results were P=0.001 (P <0.05).

4. DISCUSSION

Kumar et al. reseach on ovarian cancer therapy shows differences in hemoglobin levels before the first and after the sixth chemotherapy were because of how paclitaxel and cisplatin were cytotoxic drugs that induced myelosuppression by directly impairing hematopoiesis in the bone marrow [15]. Cisplatin enters the bone marrow cells passively through an intracellular transport mechanism. Cisplatin increase ROS production in cells and accumulation of ROS will induce cytochrome-c release from mitochondria through activation of c-Jun-N-terminal kinase and protein 38 Mitogen-activated protein kinase [16]. Cisplatin causes damage to the mitochondria through the mechanism of crosslinking in the DNA and thus interferes with cell replication and transcription. Cytochrome-c then activates caspases 8, 9, and 3 which cause apoptosis or disruption of bone marrow progenitor cell development. These developmental disorders will cause side effects in the form of decreased production of hematopoietic cells, which will ultimately affect the production of hemoglobin, leukocytes, and platelets [17].

Paclitaxel enters blood vessels and immediately distributed to target organs including the bone marrow compartment. Paclitaxel will penetrate the bone marrow cell membrane and interact with regulatory molecules in the cytoplasm then induce p53 and Cyclin Dependent Kinase Inhibitors in the nucleus thereby inhibiting cell proliferation. An increase in pro-apoptotic factors (Bax, Bak, Bim, Bok, Bad) and a decrease in anti-apoptotic factors (Bcl-2 and Bcl-x) in the mitochondria because activation of cytochrome-c and caspase 9 resulting in the process of apoptosis or disruption of the development of bone marrow progenitor cells. Impaired development of progenitor cells will affect the hematopoietic process afterall [10]. This study lacks of interpretation of other factor that might affect hemoglobin levels such as dietary factors, varieties of ages and genders in sample research, etc so further study is needed.

5. CONCLUSION

The mean hemoglobin level in nasopharyngeal cancer patients was 13.397 g /dL before cisplatin-paclitaxel chemotherapy and 11.35 g/dL after cisplatin-paclitaxel chemotherapy. There were significant differences in the mean hemoglobin levels before and after cisplatin-paclitaxel chemotherapy in nasopharyngeal cancer patients at Prof. Dr. Margono Soekarjo Hospital (P=0.001).

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